EXHIBIT 16

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By facsimile with
Confirmation by
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For the attention of the Board of Appeal

Your ref.: 97 917 856.3 – 2403
Our ref.: B06539 - CA/GCo
Lyon, 7th April 2008

"METHOD FOR PREVENTING HIV-1 INFECTION OF CD4+ CELLS"
EUROPEAN PATENT APPLICATION N° 97917856.3
REGIONAL PHASE OF PCT/US 97/05597 FILED ON 02/04/1997
IN THE NAME OF PROGENICS PHARMACEUTICALS, INC.

RE: STATEMENT SETTING OUT GROUNDS OF APPEAL (ARTICLE 108 EPC)

Dear Sirs,

Further to the Notice of Appeal filed on 25th January 2008, on behalf of Applicant, Progenics Pharmaceuticals Inc., we hereby file a written statement setting out the grounds of Appeal in accordance with Article 108 EPC.

Yours faithfully,

Applicants: Graham P. Allaway et al.
Serial No.: 09/888,938
Filed: June 25, 2001
Exhibit 16

C Almond.

Carol ALMOND-MARTIN
Professional representative
Before the European Patent office

Enc. - Statement setting out grounds of appeal;
Main Request (Clean Copy)
Main Request (Marked-up Copy)
Publication : Hill et al. (with confirmation only)
- Form 1037.

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PROGENICS PHARMACEUTICALS, INC.

Statement of Appeal under Article 108 EPC

We refer to the Decision of the Examining Division dated 26th November 2007 refusing the present European patent application, and to the Notice of Appeal filed by Applicant (Progenics Pharmaceuticals, Inc.) on 25th January 2008. The present submissions constitute Applicant's **Statement of Appeal** under Article 108 EPC.

1. Requests

Applicant hereby files a new Main Request (Claims 1 to 31). It is requested that the Decision of the Examining Division be set aside and that the Patent be maintained on the basis of the enclosed new Main Request.

Oral Proceedings are also requested under Article 116 EPC, should the Board not intend to maintain the patent on the basis of the Main Request.

2. Cited documents

In addition to documents D1 to D9 cited during the Examination Proceedings, Applicant will refer in the present Statement of Appeal to the following document, a copy of which is enclosed :

D10 : Hill, C.M. et al. Virology, 248, 357-371 (1998)

3.1 Article 123(2) EPC

Applicant submits that the claims of the new Main Request are in conformity with Article 123(2) EPC.

The new Main Request differs from Auxiliary Request 1 as filed during Oral Proceedings before the Examining Division on 7th November 2007 by the addition of new dependent claims 2 and 3, renumbering of subsequent claims, and adjustment of claim dependencies, as can be seen from the enclosed marked-up copy. Claim 1 of the new Main Request is identical to that of previous Auxiliary Request 1.

In its Decision dated 26th November 2007, the Examining Division has not explicitly indicated its finding with regard to the allowability of Claim 1 of Auxiliary Request 1 under Article 123(2) EPC. However, it can be seen from the Minutes of the Oral Proceedings (page 2, lines 20 to 22) that the claims of Auxiliary Request 1 were found to meet the requirements of Article 123(2) EPC.

Applicant submits that this finding therefore applies to Claims 1 and 4 to 29 of the new Main Request, in so far as they are identical to the claims examined by the Examining Division.

With regard to newly added claims 2 and 3 of the Main Request, support can be found in the application as filed as follows :

- Claim 2 : page 11, lines 25 to 27, and page 18, lines 19 to 21 ;
- Claim 3 : page 18, line 22.

The claims of the Main Request therefore meet the requirements of Article 123(2) EPC.

3.2. Novelty of the Main Request :

3.2.1 The Decision of the Examining Division with regard to Novelty:

The Examining Division found that Claim 1 of Auxiliary Request 1 (now Claim 1 of the Main Request) lacks novelty under Article 54(3) EPC over D4 (WO 97/45543).

In particular the Examining Division considered that D4 discloses at page 21, lines 22 to 24 and lines 2 to 5, monoclonal antibodies that bind CCR5 and block env-mediated membrane fusion,

and referred to Example 4 of D4 as a demonstration that such an antibody "works"[1]. The Examining Division stated that D4 discloses antibodies directed to the same antigen as that recited in Claim 1 of the Auxiliary Request (now Claim 1 of the Main Request), and which "inhibit HIV-1 infection". According to the ED, the features "expressed" and "receptor" are features of the antigen but not *prima facie* of the antibody, and could be regarded only as distinctive if they confer specific technical features to the antibody, which according to the ED, does not appear to be the case.

3.2.2 The subject matter of the claims of the Main Request is novel over D4 (WO 97/45543) :

Applicant contests the finding of the Examining Division with regard to the novelty of claim 1 of the Main Request (which is identical to Claim 1 of Auxiliary Request 1 filed during Oral Proceedings)[2].

In particular, Applicant submits that the Examining Division has disregarded both the terms of the claim with respect to the inhibitory properties of the antibodies and has misapprehended the extent of the technical teaching of document D4.

As will be shown below, the antibodies claimed according to Claim 1 of the Main Request represent a previously undisclosed sub-set of the general class of antibodies disclosed in D4, and are distinguished from this larger class of antibodies by i) the target cell in which they inhibit infection and ii) the type of virus which is inhibited.

i) The subject matter of the claims of the Main Request differs from the disclosure of D4 by the target cell :

Claim 1 of the Main Request requires that the monoclonal antibodies be capable of "*inhibiting infection of a human CD4+ cell by a HIV-1 virus*". Claim 1 thus requires that the "target cell" be a **human CD4+ cell** which is susceptible to infection by HIV-1 virus.

[1] As discussed in detail in section 3.2.2 (iii) below, the Examining Division is mistaken in its reading of Example 4 of D4. This example relates to polyclonal antibodies, not monoclonal antibodies, and, contrary to the Examining Division's statement, many of them did not "work".

[2] Applicant submits that the claimed subject matter is distinct from that disclosed in D4 for the reasons set out in this Statement. Applicant further submits that the relevant disclosure of D4 is not entitled to the priority date. Further comments may be provided in this respect later in the proceedings if necessary.

Applicant submits that document D4, in so far as its disclosure has a counterpart in the priority document, neither explicitly nor implicitly discloses monoclonal antibodies which are capable of inhibiting infection of a **human CD4+ cell** by a HIV-1 virus.

The only disclosure of D4 which has a counterpart in the priority document and which relates to monoclonal antibodies which have the ability to inhibit fusion between a "*target cell*" and HIV, is found in the passage at page 21 lines 1 to 24 of D4. With regard to the "target cells", this passage states as follows:

> "*...antibodies that bind CCR5 that block env-mediated membrane fusion (i)* ***associated with HIV entry into a human CD-4 positive target cell....***"
>
> *[D4, page 21 lines 2 to 3, emphasis added]*

This passage generally refers to a "human CD-4 positive target cell". It is absolutely clear from the disclosure of D4 as a whole that "*human CD-4 positive target cell*" as recited at page 21 of D4 encompasses **non-human target cells which have been engineered to express human CD4.** This is explicitly confirmed in the general description of the invention in D4 which relates to a non-human animal model useful for studying HIV infection :

> *"In accomplishing these and other objects, there has been provided, in accordance with one aspect of the present invention a stable,* ***nonhuman cell line****, the cells of which contain DNA encoding CCR5. In accordance with another aspect of the invention a* ***transgenic non-human mammal*** *is provided comprised of cells that coexpress human CD4 and CCR5.*
>
> [D4, page 4, lines 10-14 ; D4 priority document, page 4, lines 3 to 10, emphasis added]

> *"In another embodiment, the present invention relates to transgenic animals having cells that coexpress human CD4 and CCR5. Such transgenic animals represent a model system for the study of HIV infection and the development of more effective anti-HIV therapeutics.*
> *The term "animal" here denotes all mammalian species* ***except human****"*
>
> [D4, page 18, line 14 to 17 ; D4 priority document, page 8, lines 19 to 25, emphasis added]

In particular, it is noted that, as examples of "target cells" in which the antibodies of the invention can block env-mediated membrane fusion, D4 discloses at page 21 lines 21 to 23, the following cell types : "*Mv 1 lu, NIH 3T3, BS-C-1, HEK23 cells and primary human T-cells and macrophages*". However, the corresponding passage of the priority document (page 11 lines 7 to 8 of priority document) discloses only Mv 1 lu, NIH 3T3, BS-C-1 cells as target cells. These cells are cell-lines of **mink, mouse and monkey** origin, respectively. They are not human CD4+ cells as required by claim 1 of the Main Request.

Likewise, at page 16, lines 15 to 26, D4 provides further examples of cell lines suitable for expression of human CD4 and CCR5 :

> *"Cell Lines*
> *In one embodiment, the present invention relates to stable recombinant cell lines, the cells of which express CCR5 polypeptide or coexpress human CD4 and CCR5 and contain DNA that encodes CCR5. Suitable cell types include but are not limited to cells of the following types: NIH 3T3 (Murine), Mv 1 lu (Mink),BS-C-1 (African Green Monkey) and human embryonic kidney (HEK) 293 cells. Such cells are described, for example, in the Cell Line Catalog of the American Type Culture Collection (ATCC). These cells can be stably transformed by a method known to the skilled artisan"* *[D4, page 16, lines 15 to 21].*

Importantly, the corresponding disclosure of the D4 priority document, is entitled "***Nonhuman cell lines***", not "***Cell lines***" as found in the PCT application, and recites only the non-human Mv 1 lu, NIH 3T3, BS-C-1 cell-lines. There is no mention of human embryonic kidney cell lines, or any other human CD4+ cells, in this passage of the priority document.

The parts of D4 which are entitled to the priority date and which relate to monoclonal antibodies, thus do not disclose human CD4+ cells, susceptible to infection by HIV-1, as "target cells".

D4 thus at best discloses a general class of antibodies including both monoclonal and polyclonal antibodies, which block HIV env-mediated membrane fusion in target cells. The target cells are not specifically defined but include non-human cells engineered to express human CCR5, or to coexpress human CD4 and human CCR5.

This disclosure does not affect the novelty of Claim 1 of the present Main Request because anti-CCR5 antibodies which block HIV fusion in a non-human cell-line engineered to express human CD4 and human CCR5 do not necessarily block HIV-1 fusion to a human cell expressing human CD4 and human CCR5. Indeed, it is has been reported that the CCR5 receptor adopts different conformations in different cell types such that antibodies which bind to CCR5 expressed in a first cell do not necessarily bind to CCR5 expressed in a second cell of a different type. These conformational differences are thought to affect viral Env interaction with CCR5.

For example, the publication by ***Hill et al. (Virology, 248, 357-371 (1998))*** (copy enclosed as document **D10**) reports at pages 364 and 367 that anti-CCR5 antibodies which bound to 293T cells stably transfected with CCR5, did not bind to human peripheral blood mononuclear cells (PBMCs), which naturally express CD4 and CCR5. The authors state at page 358 of D10 :

"Additional use of the anti-CCR5 antibodies to examine the structure of CCR5 on different cell types indicates that CCR5 epitopes present on 293 cells are not available on CCR5 expressed on PBMCs. These data suggest that CCR5 may be subject to different post-translational modifications or may adopt specific conformational forms depending on the cell type in which it is expressed."

[D10 (Hill), page 358, lines 21 to 28]

The authors summarise their conclusions in the abstract at page 357 of D10 :

"We therefore analyzed binding of several anti-CCR5 monoclonal antibodies to cell lines and primary cells that express this chemokine receptor and found that whereas all antibodies bound to CCR5-transfected 293T cells, several did not bind to PBMC. The results suggest that CCR5 undergoes cell type specific modifications which may affect interaction with different HIV and SIV envelope glycoproteins."

[D10 (Hill), page 357, Abstract, last four lines.]

The antibodies disclosed in D4 which block HIV env-mediated membrane fusion in some members of a general class of target cells thus do not necessarily block fusion in human CD4+ cells, and consequently do not necessarily inhibit infection of a human CD4+ cell by a HIV-1 virus, as required by the present claims.

ii) The subject matter of the claims of the Main Request differs from the disclosure of D4 by the type of virus which is inhibited :

Claim 1 of the Main Request also requires that the monoclonal antibodies be capable of "*inhibiting infection of a human CD4+ cell by a HIV-1 virus*". Claim 1 thus requires that the infection which is blocked be infection by a **HIV-1 virus**.

In its decision, the Examining Division stated that the antibodies disclosed in D4 are able to "*inhibit HIV-1 infection*" (see Decision, page 6, line 1)

This is not correct. The passage of D4 on which the Examining Division is relying to destroy novelty of Claim 1 (D4, page 21, lines 1 24) does NOT relate to antibodies which block fusion associated with HIV-1 entry, but to antibodies which block fusion associated with "HIV entry". As the Board will be aware "HIV" is a generic term encompassing "HIV-1" and "HIV-2". There is no mention of HIV-1 at page 21 of D4.

It cannot be assumed that the antibodies disclosed at page 21 of D4 which block fusion associated with "HIV" in general necessarily block fusion associated specifically with "HIV-1". Indeed, as confirmed in enclosed document **D10** (Hill), whilst HIV-1 and HIV-2 are both able to use CCR5 for entry, HIV-1 entry is dependent on N-terminal regions of CCR5 which are different from those upon which entry by HIV-2 depends. The authors of D10, referring to HIV-1 and HIV-2, conclude that "*different Envs make distinct and specific interactions with the CCR5 amino terminal domain*" (see D10, page 364, column 2, lines 42 to 46).

In view of these distinct properties, it can be concluded that antibodies which block HIV-2 fusion do not necessarily block HIV-1 fusion.

iii) D4 itself demonstrates that not all antibodies encompassed by the general class of antibodies disclosed in D4 have the properties of the sub-class of antibodies now claimed :

Importantly, Document D4 itself provides irrefutable proof that not all antibodies which bind to CCR5 are capable of blocking infection of a human CD4+ by a HIV-1 virus. Indeed, Example 4 of D4 describes the production of polyclonal antibodies to peptides corresponding to extracellular domains of CCR5. It is indicated that antibodies raised to a 28 amino acid N-terminal portion of CCR5 block membrane fusion between macrophage-tropic strains of HIV and human macrophages. The Examining Division has referred to this Example in its Decision as proof that the antibodies of D4 "work". However, the Examining Division has disregarded the corresponding Example of the priority document of D4[3] which further states :

> *"In contrast, antibodies raised against other peptide-KLH conjugates will have no effect on membrane fusion between the virus and the target cells."*
>
> [D4 Priority document, page 43, lines 20 to 23]

The polyclonal antibodies disclosed in Example 4 of D4 fall within the general class of antibodies disclosed at page 21 of D4, because at page 21, lines 12 to 15 of D4 antibodies specific for at least one extracellular portion of CCR5 are described as particularly suitable for "blocking env-mediated fusion". Nevertheless Example 4 of the priority document shows that not all these antibodies, inhibit fusion between macrophage-tropic HIV strains and human macrophages. It is noted that the antibodies of Example 4 of D4 are prepared to immunogens different from that against which the antibodies of the present claims are prepared.

[3] Note that this sentence has no counterpart in the D4 PCT application.

The monoclonal antibodies claimed in the present Main Request therefore represent a selection, or "sub-class" of antibodies which is not disclosed explicitly or inherently, within the larger known class of antibodies disclosed in D4, particularly at page 21. The claimed sub-class of antibodies is characterised by the capacity to inhibit infection of a human CD4+ cell by a HIV-1 virus. This technical effect does not occur over the whole class of antibodies disclosed in D4. In accordance with established case-law, the claimed subject matter is thus a "purposive selection" (see for example T1120/00) and the selected sub-class of antibodies is novel over D4.

It is also pointed out in this respect that the only antibodies exemplified in D4 which have a counterpart in the priority document and which are capable of blocking membrane fusion between macrophage-tropic HIV strains and human macrophages are antibodies raised to the 28 amino-acid N-terminal portion of the CCR5 polypeptide. However these antibodies are POLYCLONAL antibodies ("rabbit antisera") whereas the claims of the Main Request are directed to MONOCLONAL antibodies, and as such cannot affect the novelty of the present claims.

The subject matter of claim 1 of the Main Request therefore meets the requirements of Article 54 EPC. Consequently the remaining claims of the Main Request, which either depend on claim 1 or refer back to claim 1, are also novel.

3.2. Article 84 EPC

Claim 26 of the new Main Request is identical to Claim 1 of Auxiliary Request II filed during Oral Proceedings on 7th November 2007. This request was rejected by the Examining Division for lack of clarity under Article 84 EPC. In particular, the ED considered that the use of the chemokine binding profile "MIP-1α, MIP-1β, or RANTES" to define the receptor was not clear.

Applicant contests the decision of the ED in this regard.

First, the ED considered that at the priority date of the application, the chemokine binding profiles of the various chemokine receptors was not unequivocally resolved, and referred to the present application, page 30 line 34 to page 31 line 2, and to Samson et al (**D9** in the examination proceedings) as disclosing divergent profiles for the chemokine receptor CCR1.

This is not correct. The present application does not disclose a binding profile for CCR1. The passage bridging pages 30 and 31 of present application relates to the binding capacities of both

receptors CCR1 and CCR5, taken together, and indicates "their abilities to bind MIP-1α, MIP-1β, and RANTES". In this respect, reference is made at page 31, line 2 to several prior publications, including the Samson publication (identified as reference n°22 in the present application), which clearly disclose CCR1 as binding both RANTES and MIP-1α. The information provided in the application is entirely consistent with that in Samson et al., i.e. CCR1 binds RANTES and MIP-1α. The ED's allegation that binding profiles were ambiguous at the priority date of the application is unfounded.

Second, the ED stated that the word "or" in the phrase "MIP-1α, MIP-1β, or RANTES" as it appears in present claim 26, means that the chemokine receptor binds only one of the mentioned chemokines, and that consequently the binding profile reads on CCR3. However, there is no basis in the application as filed for this interpretation. "Or" means "each of" as it can be clearly understood in context from the application. For example, it is stated at page 11, lines 17 to 19 that a chemokine receptor means a receptor capable of binding "MIP-1α, MIP-1β, RANTES or another chemokine which blocks HIV-1 infection", and it is explicitly stated at page 20, line 15 to 17 that all three chemokines MIP-1α, MIP-1β, and RANTES inhibit fusion of HIV-1 to a target cell susceptible to infection. The receptor involved in fusion therefore binds each of the chemokines MIP-1α, MIP-1β, and RANTES.

It is also pointed out that the Samson paper (D9), which was published before the first priority date of the present application, clearly states that the CCR5 receptor is the only receptor responding to physiological concentrations of MIP-1β (Samson page 3366, column 2, first paragraph). The binding profile recited in Claim 26 is unique to CCR5, and this was clear to the skilled man at the priority date of the application.

Applicant therefore submits that the definition of the receptor in terms of chemokine binding profile in Claim 26 of the Main Request is clear, and the subject matter of this claim meets the requirements of Article 84 EPC.

6. Conclusions

It is requested that the decision of the Examining Division be set aside in its entirety and that a patent be granted on the basis of the Main Request.

C Addmond.

MAIN REQUEST

1. A monoclonal antibody, or a portion thereof, prepared against an expressed human CCR5 chemokine receptor, and wherein the antibody is capable of inhibiting infection of a human $CD4^+$ cell by a HIV-1 virus.

2. A monoclonal antibody or a portion thereof according to claim 1, wherein the human CD4+ cell is a human primary CD4+ cell and the HIV-1 virus is a primary HIV-1 virus.

3. A monoclonal antibody or a portion thereof according to claim 2, wherein the human CD4+ cell is a macrophage.

4. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4+ cells, and the HIV-1 is macrophagetropic.

5. The monoclonal antibody of any one of claims 1 to 4.

6. The monoclonal antibody portion of any one of claims 1 to 4 .

7. Use of the monoclonal antibody of claim 5 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

8.. Use of the monoclonal antibody portion of claim 6 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

9. Use of the monoclonal antibody of claim 5 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

10. Use of the monoclonal antibody portion of claim 6 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

11. A pharmaceutical composition comprising the monoclonal antibody of claim 5 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.

13. A pharmaceutical composition comprising the monoclonal antibody portion of claim 6 and a pharmaceutically acceptable carrier.

14. The pharmaceutical composition of claim 13, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.

15. A composition of matter comprising a monoclonal antibody of claim 5 linked to a compound capable of increasing the *in vivo* half-life of the antibody.

16. Use of the composition of matter of claim 15 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

17. Use of the composition of matter of claim 15 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

18. A composition of matter comprising a monoclonal antibody portion of claim 6 linked to a compound capable of increasing the *in vivo* half-life of the monoclonal antibody portion.

19. Use of the composition of matter of claim 18 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

20. Use of the composition of matter of claim 21 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

21. The composition of matter of claim 15 or 16, wherein the compound is polyethylene glycol.

22. Use of the composition of matter of claim 21 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

23. Use of the composition of matter of claim 21 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

24. A pharmaceutical composition comprising the composition of matter of any one of claims 15, 18 or 21 and a pharmaceutically acceptable carrier.

25. The pharmaceutical composition of claim 24, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.

26. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1α or MIP-1β, which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.

27. The antibody according to claim 26 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.

28. The antibody according to claim 26 or 27 which is monoclonal.

29. A pharmaceutical composition comprising an amount of the antibody of claim 26 or 27 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.

30. The antibody according to claim 26 or 27 for use in HIV-1 therapy.

31. Use of an antibody according to claim 26 or 27 for the manufacture of a medicament for inhibiting HIV-1 infection.

MAIN REQUEST

1. A monoclonal antibody, or a portion thereof, prepared against an expressed human CCR5 chemokine receptor, and wherein the antibody is capable of inhibiting infection of a human $CD4^+$ cell by a HIV-1 virus.

2. A monoclonal antibody or a portion thereof according to claim 1, wherein the human CD4+ cell is a human primary CD4+ cell and the HIV-1 virus is a primary HIV-1 virus.

3. A monoclonal antibody or a portion thereof according to claim 2, wherein the human CD4+ cell is a macrophage.

4. ~~2~~. A monoclonal antibody or a portion thereof according to claim 1 which is capable of inhibiting fusion of the HIV-1 to CD4+ cells, and the HIV-1 is macrophagetropic.

5. ~~3~~. The monoclonal antibody of any one of claims 1 to ~~or 2~~4.

6. ~~4~~. The monoclonal antibody portion of any one of claims 1 to 4 ~~or 2~~.

7. ~~5~~. Use of the monoclonal antibody of claim 5 ~~3~~ for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

8. ~~6~~. Use of the monoclonal antibody portion of claim 6 ~~4~~ for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

9~~7~~. Use of the monoclonal antibody of claim 5~~3~~ for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

10~~8~~. Use of the monoclonal antibody portion of claim 6 4 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

11~~9~~. A pharmaceutical composition comprising the monoclonal antibody of claim 5 ~~3~~ and a pharmaceutically acceptable carrier.

12~~10~~. The pharmaceutical composition of claim 11 ~~9~~, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.

13~~11~~. A pharmaceutical composition comprising the monoclonal antibody portion of claim 6 4 and a pharmaceutically acceptable carrier.

14~~12~~. The pharmaceutical composition of claim 13 ~~11~~, wherein the monoclonal antibody portion is present in an amount effective to inhibit HIV-1 infection.

15~~13~~. A composition of matter comprising a monoclonal antibody of claim 5 ~~3~~ linked to a compound capable of increasing the *in vivo* half-life of the antibody.

16~~14~~. Use of the composition of matter of claim ~~13~~ 15 for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

17~~15~~. Use of the composition of matter of claim ~~13~~ 15 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

18~~16~~. A composition of matter comprising a monoclonal antibody portion of claim 4 6 linked to a compound capable of increasing the *in vivo* half-life of the monoclonal antibody portion.

19~~17~~. Use of the composition of matter of claim 18 ~~16~~ for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

20~~18~~. Use of the composition of matter of claim ~~19~~ 21 for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

21~~19~~. The composition of matter of claim 15 ~~13~~ or 16 ~~14~~, wherein the compound is polyethylene glycol.

22~~20~~. Use of the composition of matter of claim 21 ~~19~~ for the manufacture of a pharmaceutical composition for treating HIV-1 infection.

23~~21~~. Use of the composition of matter of claim 21 ~~19~~ for the manufacture of a pharmaceutical composition for inhibiting HIV-1 infection.

24~~22~~. A pharmaceutical composition comprising the composition of matter of any one of claims 15 ~~13~~, 18 ~~16~~ or 21 ~~19~~ and a pharmaceutically acceptable carrier.

2523. The pharmaceutical composition of claim 2422, wherein the amount of the composition of matter is effective to inhibit HIV-1 infection.

2624. An antibody or a portion thereof, prepared against a chemokine receptor which binds RANTES, MIP-1α or MIP-1β, which antibody is capable of inhibiting infection of a human CD4+ cell by a HIV-1 virus.

2725. The antibody according to claim 2624 which is capable of inhibiting fusion of HIV-1 to CD4+ cells thereby inhibiting HIV-1 infection, and the HIV-1 is macrophagetropic.

2826. The antibody according to claim 26 24 or 27 25 which is monoclonal.

2927. A pharmaceutical composition comprising an amount of the antibody of claim 26 24 or 27 25 effective to inhibit fusion of HIV-1 to CD4+ cells, and a pharmaceutically acceptable carrier.

3028. The antibody according to claim 26 24 or 27 25 for use in HIV-1 therapy.

3129. Use of an antibody according to claim 26 24 or 27 25 for the manufacture of a medicament for inhibiting HIV-1 infection.
